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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,431	03/25/2005	Gregoire Prevost	117P/PCT2/US	6671

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EXAMINER	
OLSON, ERIC	
ART UNIT	**PAPER NUMBER**
1623	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,431	PREVOST ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-22,26,30-34 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-22,26,30-34 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted April 12, 2007, wherein claims 2, 18-21, 30, 33, and 38 are amended and claim 1 is cancelled. This application is a national stage application of PCT/IB03/04922, filed September 29, 2003, which claims benefit of provisional application 60/414103, filed September 27, 2002.

Claims 2-22, 26, 30-34, and 38 are pending in this application.

Claims 2-22, 26, 30-34, and 38 as amended are examined on the merits herein.

Applicant's amendment with respect to the rejection of instant claims 1, 20, 30-33, and 38 under 35 USC 112, first paragraph for lacking enablement for combinations comprising any farnesyl transferase or prodrug whatsoever, has been fully considered and found to be persuasive to remove the rejection as the claims as amended recite only specific farnesyl transferase inhibitors supported by the specification. Therefore the rejection is withdrawn.

Applicant's amendment with respect to the rejection of instant claims 1-17, 20-22, and 26 under 35 USC 112, first paragraph for lacking enablement for prodrugs of the recited compounds, has been fully considered and found to be persuasive to remove the rejection as the claims as amended are not drawn to prodrugs. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-22, 26, 30-34, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gordon et al. (PCT international publication WO00/39130, of record in the previous office action) in view of Rybak. (PCT international publication WO01/64197, of record in the previous office action) Gordon et al. discloses a pharmaceutical composition comprising one of a variety of compounds having an identical formula to formula (I) recited in instant claim 2. (pp. 2-9) Further specifically recited embodiments include the farnesyl transferase inhibitors of instant claims 3-17. (pp. 17-27) These compounds are disclosed to possess anti-tumor activity (p. 16, lines 16-29) and to be useful for inhibiting prenyl transferases including farnesyl transferase. (p. 9, lines 8-25) Gordon et al. does not disclose a pharmaceutical composition comprising a combination of compound according to structure (I) and an anthracycline, or a method of treating nasopharyngeal cancer by administering such a composition to a subject. Gordon et al. also does not disclose a pharmaceutical kit comprising such a composition according to instant claims 34 and 38.

Rybak discloses therapeutic combinations of anthracyclines and farnesyl transferase inhibitors which are effective in the inhibition of tumor cell growth. (p. 13,

lines 3-6) Preferred anthracycline derivatives include daunorubicin, doxorubicin, and idarubicin. (p. 21, lines 24-26) These compositions may be used in a method of inhibiting abnormal cell growth or treating various cancers having aberrant or mutated *ras* oncogene, (p. 22, lines 12-38) in a mammal, particularly a human. The two components may be administered either simultaneously or sequentially. (p. 23, lines 16-18)

It would have been obvious to one of ordinary skill in the art at the time of the invention to produce a pharmaceutical composition comprising a farnesyl transferase inhibitor according to Gordon et al. and further comprising an anthracycline such as doxorubicin. It would also have been obvious to administer this combination to a patient suffering from nasopharyngeal carcinoma. It would further have been obvious to prepare the composition in the form of a kit comprising a container and instructions for using he composition. One of ordinary skill in the art would have been motivated to combine the two components and to administer them to a patient suffering from nasopharyngeal carcinoma because both components were known to be useful for the treatment of cancer broadly. One of ordinary skill in the art would have reasonably expected success because both compounds were known to be useful for the same purpose. It has been held that it is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose in order to practice a third composition for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Further, with respect to the kits described in instant claims 34 and 38, a pharmaceutical kit or the patient pack comprising the same combination pharmaceutical composition in two dosage forms and directions for administering the dosage forms are all deemed obvious since they are all within the knowledge and conventional skills of pharmacologist to conveniently assist the user and prescriber for easy dispensary of the medication. Moreover, the inclusion of a package inserts including "indication and use" of the pharmaceutical composition in a pharmaceutical kit is mandated by 21 CFR 201.57 according to *Remington: The Science and Practice of Pharmacy*. Furthermore, with respect to the instructions or directions that direct one on how to use in a kit, the U.S. Court of Appeals for the Federal Circuit, *In re Ngai* 03-1524, recently rules that a kit of the prior art with a set of instructions is unpatentable (see the precedential opinion issued May 13, 2004).

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted April 12, 2007, with respect to the above rejection, have been fully considered but not found persuasive to remove the rejection. Applicants argue that neither reference teaches the combination of the specific claimed farnesyl transferase inhibitor with anthracyclines. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). N the instant case, one of ordinary skill in the art would have, upon reading the two references in

combination, realized that other farnesyl transferase inhibitors, which work by the same mechanism as the compounds disclosed by Rybak et al., can be combined with anthracyclines.

Applicants further argue that neither reference provides any expectation that the combination of the two active compounds would be useful for treating nasopharyngeal cancer, as opposed to merely being useful for treating other types of cancers recited by the references. First, it is noted that this argument concerns only claims 22, 26, and 30-33 as the remaining claims 2-21, 34, and 38 make no mention of nasopharyngeal cancer whatsoever. For these claims the claimed compositions and kits must merely be shown to have some utility, rather than the specific utility of treating nasopharyngeal cancer.

Furthermore, with respect to claims 22, 26, and 30-33, the references provide sufficient information as to the mechanism of action of the invention to allow one of ordinary skill in the art to clearly determine which tumors can be treated with a reasonable expectation of success. In particular, Rybak (p. 22, lines 12-24) discloses that the combination of a farnesyl transferase inhibitor and an anthracycline is useful for inhibiting abnormal growth of cells, including cancer cells, that display an activated *ras* oncogene, activated *ras* protein, or aberrant *ras* activation. One of ordinary skill in the art would certainly be able to determine which patients' tumors bore these particular markers. The characterization of *ras* mutation and expression in a tumor can thus be used to determine whether a particular patient is a candidate for the disclosed therapy. This additional screening is of an ordinary and routine character, and provides a

reasonable expectation of success for one of ordinary skill in the art to determine which nasopharyngeal cancers (i.e. nasopharyngeal tumors bearing mutated *ras* gene, or aberrant *ras* expression) are candidates for the claimed method of treatment. Therefore it would have been obvious to select the particular subset of nasopharyngeal cancers that bear an aberrant *ras* gene or protein for treatment with the disclosed method.

With respect to claims 34 and 38, Applicant's argument is moot as the base claims are found to in fact be obvious as discussed above. Therefore a kit containing the claimed ingredients is also obvious.

For these reasons the above rejection is maintained and made **FINAL**.

Conclusion

No claims are allowed in this application. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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